REMARKS

Claims 1-5, 13, 18-19, 21-46, 53-55 and 58-60 were pending in the present application.

Claims 1, 2, 4, 5, 18, 19, 45 and 53 have been canceled. Applicants reserve the right to prosecute the subject matter of the canceled claims in one or more related continuation, continuation-in-part, and/or divisional applications.

Claim 46 has been amended to be in independent form; the claim limitations of claim 1 from which claim 46 previously depended have been incorporated into claim 46.

Claim 54 has been amended to remove its dependency from canceled claim 43 and to be dependent from claim 46 instead.

Claim 55 has been amended to specify that the RSV is encoded by the nucleic acid of claim 46. Support for this amendment can be found in the specification at ¶0170.

New claims 241 to 247 have been added. Support for the new claims can be found in the application as originally filed.

Claim	Support
241	¶0067
242	¶0011
243	¶0011
244	¶0011
245	¶0012
246	¶0012
247	¶0091

The specification has been amended to recite SEQ ID NOs. Certain sequences that were listed in the specification were not presented in the original sequence listing. A Substitute Sequence Listing is submitted herewith to correct this oversight.

No new matter has been introduced. Claims 3, 13, 21-44, 46, 54-55, 58-60 and 241-247 will be pending upon entry of the present amendment.

ATTORNEY DOCKET NUMBER

It is noted that the attorney docket no. of record at the U.S. Patent and Trademark Office is "7382-132-999." The correct attorney docket no., however, is "**7682-132-999**" as indicated in the Transmittal Of Revocation And Power Of Attorney filed on October 27, 2005. Applicants request that the Office correct its entry for the attorney docket no. for the present case.

THE OBJECTION TO THE SPECIFICATION SHOULD BE WITHDRAWN

The Examiner has objected to the specification because SEQ ID NOs were missing in the legend to figure 20 and at pages 84 and 86-88. In view of the present amendment to the specification, Applicants request that the objection to the specification be withdrawn.

THE DOUBLE PATENTING REJECTION

The claims have been provisionally rejected on the ground of non-statutory obviousness-type double patenting over U.S. Patent Application Nos.: 10/811,508. As this rejection is a provisional rejection, Applicants will not address this rejection at this time.

THE REJECTION UNDER 35 U.S.C. § 102(a) SHOULD BE WITHDRAWN

Claims 1, 2, 4, 5, 18, 19, 45, 46, and 53-55[1] were rejected under 35 U.S.C. § 102(a) as being allegedly anticipated by Lu *et al.* (Journal of Virology, 2002, 76(6):2871-2880; "Lu"). Lu, however, is not available as prior art against the claimed invention.

First, the instant application claims the benefit of U.S. Provisional Application Nos. 60/414,614 ("the '614 Application") filed September 27, 2002 and 60/444,287 ("the '287 Application") filed January 31, 2003. Support for the presently claimed recombinant viruses can be found in the specification of the '614 Application as set forth in the chart below. Thus, the presently pending claims are entitled to the benefit of priority of the '614 Application, which is September 27, 2002. Therefore, Lu, published in March 2002 is not a statutory bar to patentability.

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[1] Claims 1, 2, 4, 5, 18, 19, 45, and 53 have been cancelled in the present Amendment.

Claims	Examples of Support in the '614 Application
46	¶ 0006, ¶ 0020, ¶0008 to ¶0010, ¶0034 to ¶0037, ¶0041 to ¶0045, ¶ 0026, ¶ 0013, ¶ 0067, ¶ 0071; Examples 2 and 3 at ¶ 0086 to ¶ 0130;
54	¶ 0006, ¶ 0013, ¶ 0020, ¶ 0026, ¶ 0037, ¶ 0038, ¶ 0067 to ¶ 0071; Examples 2 and 3 at ¶ 0086 to ¶ 0130;
55	¶ 0007, ¶ 0013, ¶ 0014, ¶ 0026, ¶ 0042, ¶ 0045, ¶ 0049 to ¶ 0055, ¶ 0060 to ¶ 0061; Examples 2 and 3 at ¶ 0086 to ¶ 0130; Example 4 at ¶ 0131 to ¶ 0147;
241	¶ 0010, ¶ 0026, ¶ 0033, ¶ 0034 to ¶0035, ¶ 0037; Example 2 at ¶ 0086 to ¶ 0105;
242	¶ 0008 to ¶ 0010, ¶ 0026, ¶ 0034 to ¶ 0037, ¶ 0041 to ¶ 0045, Examples 2 and 3 at ¶ 0086 to ¶ 0130;
243	¶ 0008, ¶ 0026, ¶ 0034 to ¶ 0037; Example 2 at ¶ 0086 to ¶ 0105;
244	¶ 0008, ¶ 0026, ¶ 0034 to ¶ 0037; Example 2 at ¶ 0086 to ¶ 0105
245, 246	¶ 0009, ¶ 0026, ¶ 0041 to ¶ 0045; Example 3 at ¶ 0106 to ¶ 0130;
247	¶ 0016, ¶ 0026, ¶ 0035 to ¶ 0037, ¶ 0041 to ¶ 0045, ¶ 0051;

Second, Lu describes Applicants' own work (M.P.E.P. 715.01(d)) as it was co-authored by Hong Jin, Bin Lu, and Xing Cheng, three of the four currently listed inventors. To support this contention, Applicants will provide a Declaration Under 37 C.F.R. § 1.132 ("Declaration") as evidence that Lu is the publication of the inventors which occurred less than one year prior to the effective filing date of the present application. *In re Katz*, 687 F.2d 450, 215 U.S.P.Q. 14 (C.C.P.A. 1982).

Applicants contend that Lu is not available as prior art for any purpose under 35 U.S.C. § 102 and request that Lu be withdrawn as prior art against the present application.

THE REJECTION UNDER 35 U.S.C. § 102(b) SHOULD BE WITHDRAWN

Claims 1, 2, 4, 5, 18, 19, 45, 46, and 53-55[2] were rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by Marriott *et al.* (Journal of Virology, 1999, 73(6):5162-5165; "Marriott"). Applicants disagree as set forth in detail below.

[2] See Footnote 1 above.

THE LEGAL STANDARD

Anticipation requires that the same invention, including each element and limitation of the claims, was known or used by others before it was invented by the patentee. *Hoover Group, Inc. v. Custom Metalcraft, Inc.*, 66 F. 3d 299, 302 (Fed. Cir. 1995). An anticipating reference must describe and enable the claimed invention, including all the claim limitations, with sufficient clarity and detail to establish that the subject matter already existed in the prior art and that its existence was recognized by persons of ordinary skill in the field of the invention. *In re Spada*, 911 F.2d 705 (Fed. Cir. 1990); *Crown Operations International, Ltd. v. Solutia Inc.*, 289 F.3d 1367, 1375 (Fed. Cir. 2002).

The standard for an anticipatory reference is set forth in *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987): "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *See also Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 (Fed. Cir. 1989)(holding that "[t]he identical invention must be shown in as complete detail as is contained in the . . . claim"). Further, the anticipating reference must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating subject matter. *PPG Industries, Inc. v. Guardian Industries Corp.* 75 F. 3d 1558 (Fed. Cir. 1996).

MARRIOTT DOES NOT TEACH ALL THE CLAIM LIMITATIONS

The presently pending claims are directed to nucleic acids encoding recombinant respiratory syncytial viruses having an attenuated phenotype and in which the phosphoprotein comprises at least one mutated amino acid residue. In contrast, Marriott describes nucleic acids encoding components of the viral replication machinery, not nucleic acids encoding a virus. In particular, Marriott tested the effect of a mutation in the RSV P protein in the so-called plasmid-driven minigenome RNA transcription-replication assay. In Marriott's assay, the four proteins of the RSV replication complex, the N, P, L, and M2 proteins, are co-expressed in a host cell under the control of the promoter for the T7 RNA polymerase. Once expressed, the RSV replication complex catalyzes the transcription of RNA from pCAT-LUC, a construct that includes the two reporter genes chloramphenicol acetyltransferase (CAT) and luciferase (LUC) flanked by untranscribed regions of the RSV genome. The activity of the RSV replication complex is then monitored using the activity of CAT and

LUC as read-out. Using this assay system, Marriott tested the effect of a mutation in the P protein on the activity of the RSV replication complex. Marriott does not, however, disclose a nucleotide sequence encoding a *virus* in which the P protein is mutated.

In summary, because Marriott does not disclose a nucleotide sequence encoding a *virus* in which the P protein is mutated, Marriott fails to teach all the limitations of the rejected claims. Applicants therefore request that the rejection of claims 46 and 54-55 under 35 U.S.C. § 102(b) should be withdrawn.

THE REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, SHOULD BE WITHDRAWN

Claims 1, 2, 18, 19, and 45[3] were rejected under 35 U.S.C. § 112, first paragraph, because the specification allegedly fails to provide enabling support for these claims. Applicants respectfully disagree as set forth in detail below. Although these claims are no longer pending Applicants have nevertheless addressed these rejections in the event the Examiner deems them to be applicable to the amended claims or the new claims.

THE LEGAL STANDARD

The test for enablement is whether one reasonably skilled in the art could make or use the invention, without undue experimentation, from the disclosure in the patent specification coupled with information known in the art at the time the patent application was filed. *U.S. v. Telectronics Inc.*, 857 F.2d 778, 8 USPQ2d 1217 (Fed. Cir. 1988). In fact, well known subject matter is preferably omitted. See *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986) ("a patent need not teach, and preferably omits, what is well known in the art."). Further, one skilled in the art is presumed to use the information available to him in attempting to make or use the claimed invention. See *Northern Telecom, Inc. v. Datapoint Corp.*, 908 F.2d 931, 941 (Fed. Cir. 1990) ("A decision on the issue of enablement requires determination of whether a person skilled in the pertinent art, using the knowledge available to such a person and the disclosure in the patent document, could make and use the invention without undue experimentation."). These enablement rules preclude the need for the patent applicant to "set forth every minute detail regarding the invention."

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[3] Claims 1, 2, 18, 19, and 45 have been cancelled in the present Amendment.

Phillips Petroleum Co. v. United States Steel Corp., 673 F. Supp. 1278, 1291 (D. Del. 1991); see also *DeGeorge v. Bernier*, 768 F.2d 1318, 1323 (Fed. Cir. 1985).

Undue experimentation is experimentation that would require a level of ingenuity beyond what is expected from one of ordinary skill in the field. *Fields v. Conover*, 170 USPQ 276, 279 (CCPA 1971). The factors that can be considered in determining whether an amount of experimentation is undue have been listed in *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Among these factors are: the amount of effort involved, the guidance provided by the specification, the presence of working examples, the amount of pertinent literature and the level of skill in the art. The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, so long as it is merely routine. *Id.*

Further, while the predictability of the art can be considered in determining whether an amount of experimentation is undue, mere unpredictability of the result of an experiment is not a consideration. Indeed, the Court of Custom and Patent Appeals has specifically cautioned that the unpredictability of the result of an experiment is not a basis to conclude that the amount of experimentation is undue in *In re Angstadt*, 190 USPQ 214 (CCPA 1976), at 218-219:

> [If to fulfill the requirements of 112, first paragraph, an applicant's] disclosure must provide guidance which will enable one skilled in the art to determine, with reasonable certainty before performing the reaction whether the claimed product will be obtained, ... then all "experimentation" is "undue" since the term "experimentation" implies that the success of the particular activity is uncertain. Such a proposition is contrary to the basic policy of the Patent Act. *Id.* at 219.

Thus, all that is required is a reasonable amount of guidance with respect to the direction of the experimentation; reasonable certainty with regard to the outcome of the experimentation is not required.

In addition, the Patent and Trademark Office bears the initial burden of establishing a *prima facie* case of non-enablement. *In re Marzocchi*, 169 USPQ 367, 369 (C.C.P.A. 1971); M.P.E.P. § 2164.02. A patent applicant's specification which contains a teaching of how to make and use the invention must be taken as enabling unless there is reason to doubt the objective truth of the teachings which must be relied on for enabling support. *Id.*

Further, "if any use is enabled when multiple uses are disclosed, the application is enabling for the claimed invention." M.P.E.P. § 2164.01(c).

THE CLAIMS ARE ENABLED BY THE INSTANT SPECIFICATION

The application provides sufficient guidance for the identification of P gene mutants that result in an attenuated phenotype (claim 45).

At ¶67, the specification teaches a routine assay that can be used to identify mutations in the P protein that confer a temperature-sensitive N-P interaction. This assay is described in more detail at ¶¶230-232. Immunoprecipation and yeast-two-hybrid system are taught for the identification of mutants that affect the N-P protein-protein interaction. P protein mutants that are identified can then be further characterized using the minigenome replication assay, which is described at ¶233. At ¶244, it is taught that a temperature-sensitive N-P interaction is correlated with a temperature-sensitive phenotype in the minigenome replication assay. And ultimately, the effect of the P gene mutants on recombinant viruses can be tested using recombinant genetics as described at ¶234. At ¶249, it is taught that the effect of the phosphoprotein mutants in the minigenome replication assay correlated with the effect of these mutations in recombinant viruses. In summary, the application teaches that phosphoprotein mutations can be identified using a routine N-P protein-protein interaction assay, subsequently the function effect of the mutations can be characterized in a minigenome replication assay, and ultimately, reverse genetics can be used to demonstrate the attenuating effect of these mutations on the virus. Tests for attenuated RSV are disclosed at ¶169, and are routine in the art. Each of these assays is routine, and does not require more than standard work. It is well-established case law, that a routine assay, even if significant testing would be involved, does not constitute undue experimentation. Further, simply because the outcome may be unknown, *i.e.*, in the present case some mutations in the phosphoprotein may not result in an attenuated phenotype, does not by itself render any experimentation required to identify the mutations that are within the claim scope undue.

The specification teaches at ¶76 that proper phosphoprotein phosphorylation is required for proper viral replication in certain host cells. Illustrative tests to determine the degree of phosphorylation of the phosphoprotein are described, *e.g.*, ¶¶264 and 274. Thus, mutations can be introduced by routine molecular biology techniques, such as random mutagenesis, and candidate mutants tested via the disclosed assays. At ¶77, it is taught that the dephosphorylation of the phosphoprotein reduces N-P protein-protein interaction. ¶78 teaches that P protein phosphorylation affects viral RNA transcription and replication.

Further, ¶79 teaches that phosphoprotein phosphorylation also affects viral attenuation in mice and cotton rats.

The Examiner argues that the present claims are not enabled because the effect of similar substitutions has not been proven (Office Action of December 11, 2006, at p. 8). It is noted that the legal standard for enablement does not require certainty. On the contrary, all that is required is sufficient guidance such that the skilled artisan can perform the claimed invention without undue experimentation. As set forth above, the specification provides ample guidance for making and testing the mutations. Such routine assays are not *undue* experimentation. *See, e.g., In re Wands*, 858 F.2d 731 (Fed. Cir. 1988).

In *Wands*, antibodies that were required to perform the claimed immunoassays were held to be enabled even though only a small percentage of hybridomas were proved to fall within the claims. *Id.* at 739. In *Wands* routine assays could be used to identify the suitable hybridomas. Similarly, in the present situation, routine assays can be used to identify among the mutated recombinant RSV of the invention, those that have an attenuated phenotype. In contrast to *Wands*, however, where hybridomas were generated randomly, the present specification even provides guidance for the rational design of modifications that affect different aspects of the recombinant virus. Thus, the present application not only meets but even exceeds the legal standard for enablement.

Accordingly, Applicants have provided sufficient guidance for the skilled artisan to identify other mutations in the phosphoprotein that fulfill the requirements of the claims. Any rejection under 35 U.S.C. § 112 would therefore be inapposite.

CONCLUSION

Entry of the present amendments and consideration of the remarks made herein is respectfully requested. The Examiner is invited to contact the undersigned with any questions concerning the foregoing.

Respectfully submitted,

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Date: June 11, 2007

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